

Contralateral functional connectivity of temporal lobes in Alzheimer's disease and semantic dementia

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Introduction: The hippocampus (Hp) is the core region of atrophy in Alzheimer's disease (AD), leading to episodic memory deficits in patients. In semantic dementia (SD), degeneration of the temporal pole (Tp) has been found to contribute to the typical semantic memory deterioration (Galton, 2001). Besides, the Hp is affected also in SD, despite relatively spared episodic memory abilities (Good, 2002). Recent studies on network connectivity including these two core regions showed mainly decreased functional connectivity (fc) of the Tp in SD (Guo, 2013), and of the Hp as part of networks relevant for episodic memory processes in AD (Allen, 2007). Yet other studies have suggested that neuronal loss is accompanied by cortical reorganization which might reflect compensatory processes to maintain cognitive functioning to some degree (Kenny, 2012). The influence of such neuroplasticity mechanisms of the Hp and Tp in AD and SD are not well understood. To this end, the present study investigated the fc of the Hp and the superior Tp in AD and SD as compared to healthy elderly controls (EC).

Methods: We analyzed resting-state fMRI data from 15 patients with early AD (mean age 68, range 53–83; mean MMSE 25.1, range 13–28), 5 with SD (age 64, 56–69; MMSE 21.4, 14–27), and 19 EC (age 68, 62–73; 28.8, 27–30) after excluding 5 subjects with head movements (3 AD, 1 SD, 1 EC). The reason for the small SD group was its rare prevalence. Data were acquired with a 3T scanner, using an EPI sequence (400 volumes, 26 slices, 3.0 x 3.0 x 4 mm³, TR/TE 1600ms/35ms). Preprocessing was performed in SPM8 and included slice-time correction, realignment, coregistration, normalization, and smoothing (FWHM 8 mm). Data was high-pass filtered (1/128 Hz) and we modeled 14 nuisance parameters (6 movement parameters and its first derivative, white matter, and CSF). For the fc analysis, we extracted time-series from 7 AAL ROIs from the temporal lobe (Fig. 1B) to calculate Pearson correlations. Further, the signal from the two core regions superior Tp and Hp were subjected to a seed-based whole brain analysis.

Results: We compared temporal lobe fc among groups and found twice as many regions with a high ipsilateral fc in the right hemisphere in SD (temp. lobe right 6; left 3) and AD (right 5; left 3) as compared to the left hemisphere (Fig. 1A). Moreover, both patient groups demonstrated contralateral fc (SD 3; AD 2). In contrast, EC showed a symmetric fc pattern across both hemispheres. To compare the two patient groups, we performed Wilcoxon rank-sum tests that demonstrated the largest group effect between SD and AD, which was a 20% reduction in fc strength in SD patients between the left superior and left temporal gyrus ($W = 28$, $p = 0.036$, see Fig. 1A). Whole-brain analysis with Hp as seed showed lower fc in the temporal pole in AD compared to EC (Fig. 2A). With Tp as seed, SD exhibited a more distributed fc pattern than the other groups, who mainly showed insular fc (Fig. 2B).

Discussion: The strongest connected regions of the seven ROIs in the EC group can be found ipsilateral. This favors the view of a distinct functional differentiation of the hemispheres, which is common in healthy adults. Brain regions affected by atrophy, however, appear to reorganize the functional network by recruitment of not only proximate and more preserved, but also distal regions such as contralateral temporal regions as found in the patient groups of this study. Furthermore, the case of SD showed that the less atrophied right temporal lobe generates more and stronger connections, possibly to compensate for the damage in the left hemisphere. Taken together, our results suggest that despite a decrease of fc in degenerated brain areas shown in numerous studies before, the preserved tissue appears to strengthen the connection to other regions previously not connected as strongly. This mechanism might reflect the reorganization of functional networks in AD and SD, which could improve personalized therapy.

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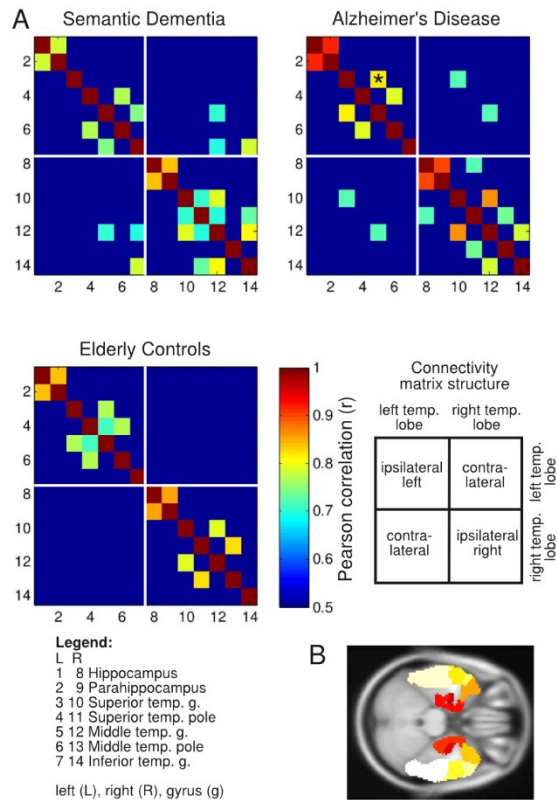


Fig. 1: (A) Temporal functional connectivity in the three groups. Median Pearson correlation as connectivity strength (only $r > 0.7$ are shown which corresponds to 50% shared variance between two regions, all $p < .001$, corrected for 91 test). **(B)** Seven ROIs from AAL atlas (superior temporal gyrus ROI not visible in this slice).

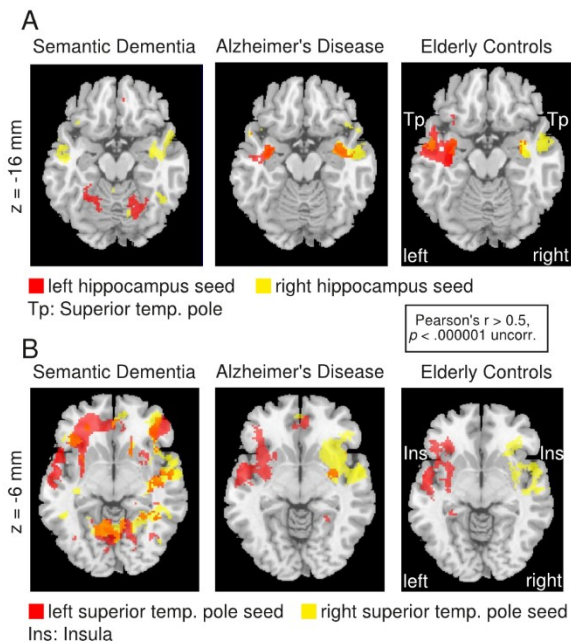


Fig. 2: Seed-based whole-brain connectivity of left and right hippocampus (A) and superior temporal pole (B).